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PATENT APPLICATION
Docket No.: NC 79,856

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of: Feldstein
Serial No.: 09/917,649
Filed: 07/31/2001
For: FLUIDICS SYSTEM
Examiner: Ludlow, Jan M.
Art Group Unit: 1743

Honorable Commissioner of Patents
PO Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. § 1.131 OF MARK J. FELDSTEIN

Sir:

I, Mark J. Feldstein, hereby declare that:

1. I am the inventor of the invention claimed in the above-identified patent application.

2. Attached is a copy of portions of my invention disclosure, which formed the basis of this patent application.

3. The Certification of Inventors shows my signature, which was in fact, to the best of my recollection, signed on 05/03/1999 as shown. The contents of the disclosure were complete at the time that I signed it.

4. All work described in the disclosure was performed by me or under my supervision, no later than 05/03/1999 in a NAFTA or WTO member country.

5. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

December 7, 2005
Date

Mark J. Feldstein
Mark J. Feldstein

79,856

INSTRUCTIONS: A Navy employee should use this form when submitting an invention disclosure to the Department of the Navy. Fill in each blank with the requested information or enter "NONE" as appropriate. Original and two copies should be printed or typed and forwarded to the intellectual property office responsible for providing services to your activity. Where space on form is inadequate, enter "see attached page," use plain pages as needed, and identify item by number. When completely executed, this form becomes an important legal document useful in proving priority of invention. This form may also be used by a contractor or grantee for disclosing an invention to the Navy.

PART 1. RECORD OF INVENTION

1. INVENTOR(S)	ADDRESS	POSITION TITLE	EMPLOYER (Activity & Code No., or Company & address)
Mark J. Feldstein	436 6th street, NE Washington, DC 20002	NRC Postdoc	Code 6910

2. DESCRIPTIVE TITLE OF INVENTION

Pressure Relief Vent Fluid Control for Miniature Fluidics Devices

3. CONCEPTION, INITIAL RECORDS AND RESULTS OF FIRST MODEL

a. EARLIEST DATE AND PLACE INVENTION WAS CONCEIVED *(Identify persons and records to support date and place)*

Reduced to practice 12-18-98, see note book of Feldstein

b. DATE AND PRESENT LOCATION OF FIRST SKETCH, DRAWING OR PHOTO AND FIRST WRITTEN DESCRIPTION *(Such as notebook entries, etc.)*

First sketch 12-17-98, see notebook of Feldstein (page 139)

c. DATE AND PLACE OF COMPLETION OF FIRST MODEL, PROTOTYPE, PRELIMINARY SYNTHESIS, FORMULATION, ETC., AND ITS PRESENT LOCATION

First reduction at NRL code 6910, Bldg 30, Rm 130 12-17-98

d. DATE AND PLACE OF FIRST TEST OR OPERATION AND THE RESULTS *(Give name and address of witnesses, and present location of records)*

NRL code 6910, bldg 30, rm 130: 12-17-98

4. OTHER RECORDS *(Notebook entries, descriptions, reports, drawings, etc.)*

IDENTIFICATION	DATE OF DOCUMENT	PRESENT LOCATION
Additional reduction 4-29-99 showing functioning of system with results measured using fluorescence spectrometer	4-29-99	NRL code 6910

5. OTHER INDIVIDUALS TO WHOM INVENTION WAS DISCLOSED

NAME	ACTIVITY OR COMPANY INDIVIDUAL REPRESENTS	DATE DISCLOSED	TYPE (oral or written disclosures)
Fran Ligler	NRL Code 6910	12-18-98	Oral
Joel Golden	NRL Code 6910	12-18-98	Oral/Demo
George Anderson	NRL Code 6910	4-29-99	Oral

NAVOCNR 5870/35 (11-89) Formerly NAVONR 5870/35 (Rev. 5-83)

6. DATE AND PLACE OF OTHER TESTS OR OPERATIONS, AND THE RESULTS *(List name and address of witnesses and identify present location of records)*

7. IDENTIFY ANY PAST, PRESENT OR CONTEMPLATED USE, SALE, OR PUBLICATION OF THE INVENTION

Publication to be submitted within 6 weeks.

8. LIST ANY CLOSELY RELATED PATENTS, PATENT APPLICATIONS AND PUBLICATIONS OF YOURS OR OTHER PERSONS

PART II. DISCLOSURE OF INVENTION

Attach on separate sheets of paper a full and complete description of the invention, using the outline given below.

a. PURPOSE. State the purpose of the invention.

b. BACKGROUND. Describe the old methods, materials or apparatus used to perform the purpose of the invention and give their limitations and disadvantages.

c. DESCRIPTION AND OPERATION. Describe clearly and completely the best mode of the invention and give a detailed description of its operation and use. Sketches, prints, photos, or other illustrations should be attached. In the description, use reference characters to refer to components in attached illustrations.

d. ADVANTAGES AND NEW FEATURES. State the advantages of the invention over the old methods, materials or apparatus described in paragraph b above, and the features believed to be new.

e. ALTERNATIVES. Indicate any alternative methods, materials, or apparatus of the invention.

f. CONTRIBUTIONS BY INVENTORS. If this is a joint invention, indicate what contribution was made by each inventor.

PART III. CERTIFICATION OF INVENTORS

I certify that the invention disclosed herein and in the attached documents is the ☒ sole ☐ joint invention of the undersigned and that statements and answers are true to my best knowledge and belief.

Date 5-3-99	Signature [signature]
Date	Signature
Date	Signature
Date	Signature

PART IV. CERTIFICATION OF WITNESSES

I certify that the invention described herein and in the attached documents has been disclosed to and understood by me.

Date 5/3/99	Signature [signature]	Business Address NRL CODE 6910
Date 5/3/99	Signature [signature]	Business Address NRL Code 6900

NAVOCNR 5870/35 (11-89) (Reverse)

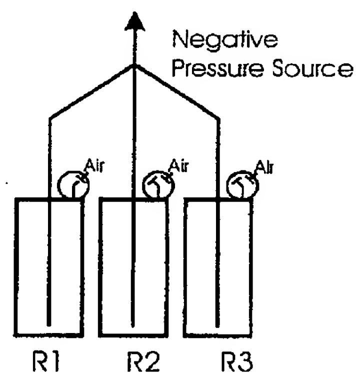
this invention to provide this control where channel sizes can be sufficiently large (cross sections greater than approximately 100 μm) that clogging due to suspended contaminants will be unlikely and where flow rates of μl/min to ml/min or greater can be achieved.

VII. DESCRIPTION OF INVENTION

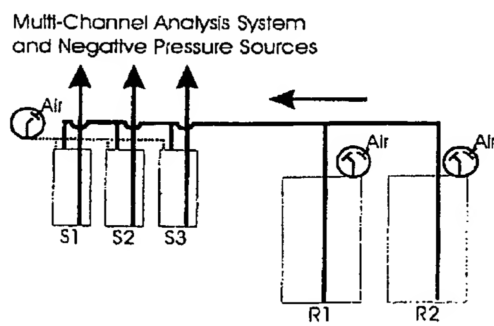
A method and apparatus for fluid selection from one or more fluid reservoirs is provided for by this invention through actuation of a pressure relief vent associated with each reservoir. Specifically, while using a single negative pressure source (e.g., pump) connected to one or more reservoirs by means of a 1-X manifold (where X is the number of reservoirs), a relief vent opens one of the previously sealed reservoirs to allow gas (e.g., air) to backfill the reservoir. If only one of the X reservoirs is open, fluid will be preferentially drawn from that reservoir given that the other reservoirs, which are sealed, will be highly resistant to fluid flow. If more than one of the reservoirs' relief vents are open to allow gas backfill, then fluid may be drawn from multiple reservoirs simultaneously. A system-wide relief vent can also be incorporated in order to disable fluid flow by providing centralized depressurization of the fluid circuit.

The unique features of this invention are that fluid selection is accomplished without passing fluids through valves and without resorting to micron-scale fluidics channels, thus circumventing the problems of valve and channel clogging due to sample contaminants. Further, the overall size and power consumption of the fluidics system is reduced, as compared to other methods, given that relatively small valves can be used for the necessary pressure relief since only gas, and not fluid, will pass through them.

An example configuration where multiple fluids can be selectively dispensed without passing though any valves is shown in Figure 1. In this embodiment, fluids from three reservoirs (R1, R2, R3) can be selectively drawn towards a single negative pressure source (ex, pump) without passing through any valves. To draw Fluid 1 from Reservoir 1, the pressure relief vent on R1 is opened to air while the pressure relief vents on R2 and R3 remain sealed (as shown). Similarly, to draw Fluid 2 (or 3) from Reservoir 2 (or 3), the pressure relief vent on R2 (or R3) would be opened to allow gas backfill while the other relief vents would be sealed. This configuration could be scaled to control any number of reservoirs.



More complex arrangements where a larger number of fluids can be selectively dispensed without passing through any valves are also possible. For example, in order to analyze three samples simultaneously in a multi-channel bio/chemical sensor where each sample requires processing with two reagents, an embodiment as shown in Figure 2 is possible. In this configuration, Samples 1, 2, and 3 (S1, S2, and S3) can be drawn into a multi-channel analysis system by opening a single pressure relief vent that is connected to all three sample reservoirs. When this relief vent is closed and the relief vent on reagent



PAGE 25/29 * RCVD AT 12/7/2005 10:24:59 AM [Eastern Standard Time] * SVR:USPTO-EFXRF-6/25 * DNIS:2738300 * CSID:202 404 7380 * DURATION (mm-ss):11-00

reservoir 1 or 2 (R1, R2) is open, the sample flow will cease and the appropriate reagent will be dispensed into each of the three samples reservoirs and then into each of the three analysis channels. In order to achieve parallel dispensing, as illustrated by this figure, each channel needs an independent negative pressure source. This configuration could be scaled to control any number of samples and reagent reservoirs.

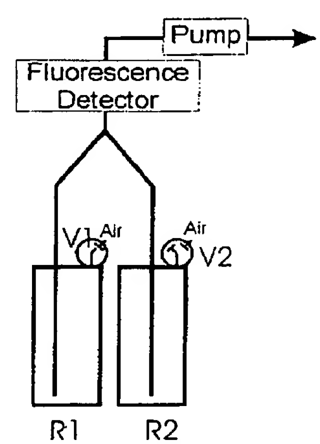
Alternate embodiments are also possible wherein the reservoirs are not merely sealed-off by relief vents but where a negative pressure is applied when they are in an 'off' position in provide greater flow resistance. This would enable fluid flow at higher pressures without risk of undesired contamination from other reservoirs. In addition, instead of using relief vents to select a *source* reservoir, the system direction could be reversed and the pressure relief vents could be used to select among *output* reservoirs. Further, positive pressure could be applied to the undesired reservoirs in order to make them more resistant to filling and thus favor a selected reservoir for fluid output.

There are some general considerations with respect to the range of fluid types, channel sizes, pump pressures, and substrate materials. The relief vent control for fluidics method operates where the resistance to flow of one given fluid, due to surface tension, channel size, channel material, etc., is less than the resistance to flow of a second fluid caused by the sealing-off of the second reservoir from the atmosphere. This difference in resistance between the flow of fluid one and two should be greater than potential of the negative pressure source at the flow rate used. A relation analogous to Ohm's law can be used to express this requirement. That is, relief vent control will operate under conditions such that: $\Delta R \leqq \Delta P/I$; where $\Delta R = R_2 - R_1$ and R_2 is resistance to fluid flow caused by sealing R_2 from the atmosphere and R_1 is the resistance to fluid flow due to factors such as fluid channel size, viscosity, channel material, etc., ΔP is the negative pressure difference from ambient that the pump can draw, and I is the flow rate.

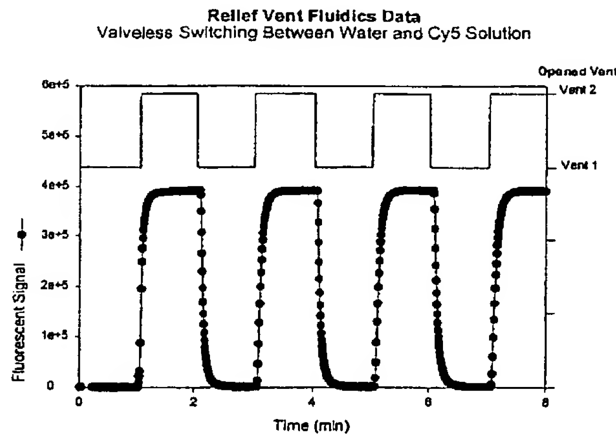
VIII. EXAMPLES

1. Two Reservoir Selection

A two-reservoir system, as shown schematically on the right, was constructed. Each glass reservoir, R1 and R2, had a fluid output connected through a T-junction into a fluorescence detector. R1 contained water and R2 contained a 60 nM aqueous solution of fluorescent dye Cy5. Each reservoir, R1 and R2, was sealed to the atmosphere except that they were connected to a micro relief vents (LFAA12034, The Lee Company), V1 and V2, respectively. The default closed position of a valve caused the given reservoir to be sealed from the atmosphere. The relief vents could be individually actuated (via a 12 volt signal) to open a given reservoir to atmospheric pressure. A peristaltic pump, running at 1.5 ml/min, was used to draw fluid from the reservoirs and through the detector to waste. In this configuration, and as described above, when V1 was open the fluid in R1 (water) would be drawn through the detector by the pump. The fluid in R2 (Cy5) would not flow because of greater resistance to flow resulting from the inability of air to backfill that reservoir. The fluid in R2 would flow, exclusively, when V1 was closed and V2 opened.



The data graph (below) shows the fluorescent signal as the valves are periodically switched open and closed. Specifically, when vent 1 is open, the signal level is essentially zero. The fluorescence detector recorded a signal level of zero when water was pulled through the system. However, when V1 was closed and V2 open the fluorescence signal rose sharply since the Cy5 solution in R2 was now pulled through the system.



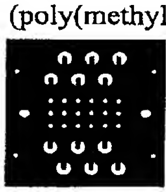
The slight delay of the signal rise as compared to the opening of vent 2 was due to the finite distance that the fluid needed to flow from the T-junction to the detector. The tailing of the signal level to zero when vent 1 was open can be attributed to the detection of residual Cy5 in the fluid channels being washed out by the water in R1.

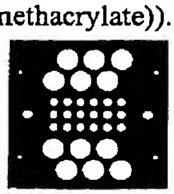
2. Microfluidics "Cube"

A second application of relief vent control for fluidics system is embodied in a fluidics "cube" only 75 cm^3 in total size. This cube contains a three-dimensional fluidics circuit and reservoirs to contain and deliver sample and labeling reagents to six different assay channels. The cube is designed to provide a variety assay formats. For example, when combined with the Array Sensor (M.J. Feldstein, J.P. Golden, C.A. Rowe, B.D. MacCraith, F.S. Ligler, "Array Biosensor: Optical and Fluidics Systems", *Biomedical Microdevices* 1(2) (1999)), six different samples can be analyzed simultaneously, each sample being analyzed for up to six different analytes. Alternately, the cube is suitable for use with another assay methodology suitable for simultaneously processing a significantly greater number of different analytes. Moreover, the interface format currently used to connect the cube to the Array Sensor system is designed to be general purpose. Thus, the cube will be suitable for connection to a variety of assay systems.

The fluidics cube is essentially a passive fluid circuit. That is, it operates without the use of any internal valves or meters. Instead, the fluid delivery relies on the relief vent control for fluidics system described herein. This unique method of fluid selection is achieved without passing the fluids through valves and without resorting to micron-scale fluidics channels. These features circumvent the problems of valve and channel clogging due to sample contaminants. Further, the overall size and power consumption of the fluidics system is reduced, as compared to other methods.

The fluidics cube is constructed from stacked layers of thermoplastic (poly(methylmethacrylate)). As shown in the accompanying figures (left) of layers 2 and 3, each layer contains a series of two-dimensional features. When aligned and annealed into a single unit, these features provide the appropriate network of fluid channels and reservoirs. The layers are fused into a single fluid-tight unit by stacking the layers together under moderate pressure and heating to just above their


Layer 2


Layer 3

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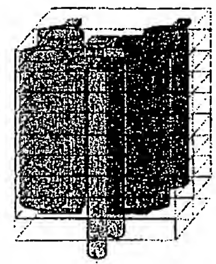
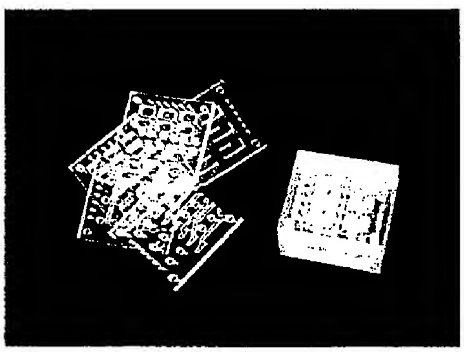
glass transition temperature.



The figure (right) depicts the three-dimensional layout of the cube achieved by stacking together and annealing the individual layers. Reservoirs and fluid channels for two sets of assays are shown. (The actual embodiment contains reservoirs and channels for conducting six independent assays.) In this configuration, one series of reservoirs (for example, the red reservoirs towards the right) are connected together to one relief vent and the second set of reservoirs (green, left) are connected to a second relief vent. Using the method of opening one relief vent to the atmosphere while maintaining the other vent closed, either set of reservoirs can be selectively draw through the central output (blue channels) of the cube and into an analysis system. The fluid cube design allows for a series of samples to be processed in parallel using only two relief vents. A photograph of the separate layers and an assembled, operation fluidics cube is shown below.



The standard cube provides reservoirs sufficient for six 0.4 ml samples and six 0.4 ml labeling reagents. The design, however, is modular. The reservoir volume and be increased or decreased, prior to annealing, in 0.2 ml increments by simply adding or subtracting certain layers of the cube.

The fluidics cube has been developed to operate with newly available miniature peristaltic pumps. Three of these pumps add a total of only 60 cm^3 to the size of the device. Further, these pumps draw minimal current (50-75 mA max per pump) making them ideally suited for extended battery operation.

IX. Advantages and New Features

The unique features of this invention are:

1. Fluid selection is accomplished without passing fluids through valves and without resorting to micron-scale fluidics channels, thus circumventing the problems of valve and channel clogging due to sample contaminants.
2. The overall size and power consumption of the fluidics system is reduced, as compared to other methods used for laboratory-scale instrumentation, given that relatively small actuators can be used for the necessary pressure relief since only gas, and not fluid, will pass through them.

The advantages of this invention are:

1. This invention addresses and solves the unique demands of compact, low power and especially portable bio/chemical analysis systems. Since the development of such systems is currently an emerging field of technology, the size and power specifications are still being developed. Many of the newly defined requirements can

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not be met by currently available fluid control methods but are met by the present invention.

2. This invention overcomes the limitations of the prior art teachings of valveless fluid control via reliance on of the unique physics of laminar flow. Laminar flow is limited to low Reynold's number situations (ex., for aqueous systems channel dimensions of less than approximately 100 μm) resulting substantial limitations not affecting the current invention.

    i. First, flow rates in the low Reynold's number regime are limited and throughputs of 100's μl/min and greater cannot be achieved through aqueous fluid through a single channel while maintaining laminar flow. Thus, laminar flow based systems are not suitable for processing within several minutes sample volumes of greater than a few μl.

    ii. Second, laminar flow based systems are not compatible with unfiltered fluid samples that may contain suspended particulates. This incompatibility arises from the use of micron scale channels in these systems and the likelihood of clogging by particualates.

X. Alternatives

1. There is no limit on the number of reservoirs that can be controlled, either in series or in parallel or combination thereof, using the disclosed method.
2. In addition to controlling fluids being selectively drawn out of different reservoirs, the disclosed method is equally applicable to controlling fluids being selectively pumped into different reservoirs.
3. The practice of the invention is not limited to reservoirs made from glass or plastic, it could be operated using reservoirs made from any material, such as a metal or ceramic, as long as the material can be effectively sealed from the atmosphere.
4. The reservoirs can be not merely sealed-off to the atmosphere by relief vents but a negative pressure could be applied when they are in an 'off' position in provide greater flow resistance. This would enable fluid flow at higher pressures without risk of undesired contamination from other reservoirs. This would also provide for greater range of functional pump pressures and flow rates.
5. If the invention is practiced to control the selection among *output* reservoirs then positive pressure could be applied to the undesired reservoirs in order to make them more resistant to filling and thus favor a selected reservoir for fluid output. This would also provide for greater range of functional pump pressures and flow rates.
6. Any suitable vent could be used, including manual, automatic. Physical and chemical vents could also be used. For example, the swelling and contracting of a polymer could function as a vent.